



D. B. Denison
#3
Patent Application
Attorney Docket No. FC11801A
10/12/03

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF: Frank Lombardo, et al.

APPLICATION NO.: 10/081,784 : Examiner: To be assigned

FILING DATE: 02/21/2002 : Group Art Unit: 2857

TITLE: TOOL FOR LIPOPHILICITY
DETERMINATION IN DRUG DISCOVERY
BASIC AND NEUTRAL COMPOUNDS

Hon. Commissioner for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

Sir:

INFORMATION DISCLOSURE STATEMENT
PURSUANT TO 37 C.F.R. § 1.97 ET SEQ and § 1.98

Pursuant to 37 CFR § 1.97 Applicants herein make available to the U.S. Patent and Trademark Office a copy of PTO-FB-A820 which lists the references cited by the Applicants, copies of which are enclosed. Applicants cite a total of 68 references, four of which are non-English language documents.

Examiner is requested to consider carefully the complete text of the 64 English language references in connection with the examination of the above-identified Application in accord with 37 C.F.R. § 1.104(a).

With respect to the four non-English language documents, since Applicants do not have in their possession, custody or control a written English translation, Applicants have herein provided in accordance with MPEP §609 III A(2) and (3) a concise explanation of the non-English document's relevance, as it is presently understood by the Applicants.

(1) Büchi, V., et al., *Zusammenhänge zwischen der chemischen Konstitution, den physikalisch-chemischen Eigenschaften, der chemischen reaktivität und der lokalanästhetischen Wirksamkeit einiger Procain-Isostere, Arzneim.-Forsch.*, Vol. 22: 1071-

1084, 1972. Page 1080 Table 3.4 of the reference cites the "Verteilungsloeffizienten" or "partition coefficient" of compound Procainamide. Applicants utilized this data to calculate the average $\log D_{oct}$ of said compound, as disclosed in Table 1 page 12 of the Application as originally filed.

(2) Graf, E., et al., *pK- und V_k-Messungen an Benzodiazepinen*, Pharm. Uns. Zeit., Vol. 6: 171-178, 1977. Page 178, lines 4-5 of the reference cites the "Verteilungsloeffizienten" or "partition coefficient" of the compound Lormetazepam. Applicants utilized this data to calculate the average $\log D_{oct}$ of said compound, as disclosed in Table 1 page 11 of the Application as originally filed.

(3) Mohler, V., et al., *On Chemistry and synthesis of 3,7-dimethyl-1-(5-oxo-hexyl)-xanthine*, Arzneim.-Forsch., Vol. 21: 1159-1160, 1971. Page 1159 of the reference cites the "Verteilungsloeffizienten" or "partition coefficient" of "BL 191" or the compound Pentoxifylline. Applicants utilized this data to calculate the average $\log D_{oct}$ of said compound, as disclosed in Table 1 page 11 of the Application as originally filed.

(4) Schutz, V., et al., *Screening, detection and biotransformation of Lormetazepam, a new hypnotic agent from the 1,4-benzodiazepine series*, Arzneim.-Forsch., Vol. 32: 177-183, 1977. Table 5 on page 178 of reference cites the "Verteilungsloeffizienten" or "partition coefficient" of the compound Lorazepam. Applicants utilized this data to calculate the average $\log D_{oct}$ of said compound, as disclosed in Table 1 page 11 of the Application as originally filed.

Examiner is requested to consider the above text taken from the non-English references in connection with the examination of the above-identified Application in accord with 37 C.F.R. § 1.104(a).

It is believed the Examiner will concur with Applicants' belief that the subject matter presently claimed is neither anticipated nor rendered obvious by the foregoing references.

It is requested that the references listed on the attached form PTO-FB-A820 be included in the "References Cited" portion of any patent issuing from this application (M.P.E.P. § 1302.12).

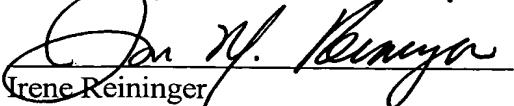
Patent Application
Attorney Docket No. PC11861A

A prompt and favorable response is earnestly solicited.

Date:

September 30, 2003

Respectfully submitted,


Irene Reininger
Attorney for Applicants
Reg. No. 48,439

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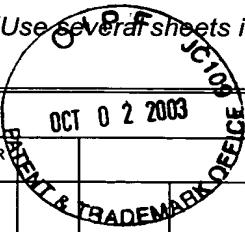
Application of _____
Frank Lombardo, et al.

Entitled
**TOOL FOR LIQUID-CHROMATOGRAPHIC DETERMINATION IN DRUG DISCOVERY BASIC
AND NEUTRAL COMPOUNDS**

The following, due _____ in the U.S. Patent and Trademark Office, has been received there on the date stamped hereon:

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INFORMATION DISCLOSURE CITATION <i>(Use several sheets if necessary)</i>			ATTY. DOCKET NO. PC11861A			SERIAL NO. 10/081,784			
			APPLICANT Frank Lombardo, et al.			FILING DATE 02/21/2002		GROUP 2857	
U.S. PATENT DOCUMENTS									
EXAMINER INITIAL <i>OCT 02 2003</i> <i>ENT & TRADEMARK OFFICE</i>	DOCUMENT NUMBER			DATE	NAME		CLASS <i>OCT 15 2003</i> <i>TC 1700</i>	SUBCLASS	FILING DATE IF APPROPRIATE
FOREIGN PATENT DOCUMENTS									
DOCUMENT NUMBER				DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
								YES NO	
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)									
		Abraham, M., et al., <i>Hydrogen bonding XXXV. Relationship between high-performance liquid chromatography capacity factors and water-octanol partition coefficients</i> , <i>J. Chromatogr.</i> , Vol. 685: 203-211, 1994							
		Adams, G., et al., <i>Structure-activity relationships in the development of hypoxic cell radiosensitizers</i> , <i>Int. J. Radiat. Biol.</i> , Vol. 35 (2): 133-150, 1979							
		Alessi-Severini, S., et al., <i>Flecainide</i> , <i>In Analytical profiles of drug substances and excipients</i> , Vol. 21: 169-195, 1992							
		Anderson, B., et al., <i>Effects of lipophilicity of nitroimidazoles on radiosensitization of hypoxic bacterial cells in vitro</i> , <i>Br. J. Cancer</i> , Vol. 39: 705-710, 1979							
		Artursson, P., et al., <i>Correlation between oral drug absorption in humans and apparent drug permeability coefficients in human intestinal epithelia (Caco-2) cells</i> , <i>Biochem. Biophys. Res. Comm.</i> , Vol. 175(3): 880-885, 1991							
		Avdeef, A., <i>Assessment of distribution-pH profiles</i> , <i>Lipophilicity in drug action and toxicology</i> , CH. 7: 110-139, 1996							
		Barbato, F., et al., <i>Hydrophobic constants and quantitative structure activity relationships (QSAR) in sets of phenothiazine drugs</i> , <i>Eur. J. Med. Chem. - Chim. Ther.</i> , Vol. 17(3): 229-234, 1982							
		Barbato, F., et al., <i>Chromatographic indices determined on an immobilized artificial membrane (IAM) column as descriptors of lipophilic and polar interactions of 4-phenylhydropyridine calcium-channel blockers with biomembranes</i> , <i>Eur. J. Med. Chem.</i> , Vol. 31: 311-318, 1996							
		Barbato, F., et al., <i>Relationships between octanol-water partition dat, chromatographic indices and their dependence on pH in a set of beta-adrenoceptor blocking agents</i> , <i>Il Farmaco</i> , Vol. 45(6): 647-663, 1990							
		Berthod, A., et al., <i>Hydrophobicity of ionizable compounds. A theoretical study and measurements of diuretic octanol-water partition coefficients by countercurrent chromatography</i> , <i>Anal. Chem.</i> , Vol. 71: 879-888, 1999							
		Büchi, V., et al., <i>Zusammenhänge zwischen der chemischen Konstitution, den physikalisch-chemischen Eigenschaften, der chemischen reaktivität und der lokalanästhetischen Wirksamkeit einiger Procain-Isostere</i> , <i>Arzneim.-Forsch.</i> , Vol. 22: 1071-1084, 1972							
		Bundgaard, H., et al., <i>Allopurinol prodrugs. II. Synthesis, hydrolysis kinetics and physicochemical properties of various N-acyloxymethyl allopurinol derivatives</i> , <i>Inter. J. Pharm.</i> , Vol. 24: 307-325, 1985							
		Camenisch, G., et al., <i>Estimation of permeability by passive diffusion through Caco-2 cell monolayers using the drugs' lipophilicity and molecular weight</i> , <i>Eur. J. Pharm. Sci.</i> , Vol. 6:313-319, 1998							
		Carelli, V., et al., <i>Enhancement effects in the permeation of Alprazolam through hairless mouse skin</i> , <i>Inter. J. Pharm.</i> , Vol. 88: 89-97, 1992							
EXAMINER		DATE CONSIDERED				RECEIVED <i>OCT 14 2003</i> TC 1700			

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				TC	1700		YES	NO
<p style="text-align: center;">OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)</p>								
<p>Carmichael, F., et al., <i>In Vitro inhibitory effects of narcotic analgesics and other psychotropic drugs on the active uptake of norepinephrine in mouse brain tissue</i>, <i>J. Pharmacol. Exp. Ther.</i>, Vol. 186(2): 253-260, 1973</p>								
<p>Fujita, T., et al., <i>A new substituent constant, π, derived from partition coefficients</i>, <i>J. Am. Chem. Soc.</i>, Vol. 86: 5175-5180, 1965</p>								
<p>Graf, E., et al., <i>pK- und π-Messungen an Benzodiazepinen</i>, <i>Pharm. Uns. Zeit.</i>, Vol. 6: 171-178, 1977</p>								
<p>Hansch, E., et al., <i>Structure-Activity relationship of chloramphenicols</i>, <i>J. Med. Chem.</i>, Vol. 16(8): 917-922, 1973</p>								
<p>Hansch, E., et al., <i>Exploring QSAR. Hydrophobic, Electronic, and Steric Constants</i>, American Chemical Society: Washington, D.C., 3-216, 1995</p>								
<p>Henczi, M., et al., <i>Determination of octanol-water partition coefficients by an HPLC method for anticonvulsant structure-activity studies</i>, <i>J. Pharm. Pharmacol.</i>, Vol. 47: 345-347, 1995</p>								
<p>Iwasa, J., et al., <i>Substituent constants for aliphatic functions obtained from partition coefficients</i>, <i>J. Med. Chem.</i>, Vol. 8: 150-153, 1965</p>								
<p>Jezequel, S., <i>Fluconazole: Interspecies scaling and allometric relationships of pharmacokinetic properties</i>, <i>J. Pharm. Pharmacol.</i>, Vol. 46: 196-199, 1994</p>								
<p>Kaufman, J., et al., <i>Microelectrometric titration measurement of the pK_a's and partition and drug distribution coefficients of narcotics and narcotic antagonists and their pH and temperature dependence</i>, <i>J. Med. Chem.</i>, Vol. 18(7): 647-655, 1975</p>								
<p>Lacko, L., et al., <i>The affinities of Benzodiazepines to the transport protein of glucose in human erythrocytes</i>, <i>Arzneim.-Forsch/Drug Res.</i>, Vol. 34(I): 403-407, 1984</p>								
<p>La Rotonda, et al., <i>Relationships between octanol-water partition data, chromatographic indices and their dependence on pH in a set of nonsteroidal anti-inflammatory drugs</i>, <i>Quant. Struct.-Act. Relat.</i>, Vol. 2: 168-173, 1983</p>								
<p>Lipinski, C., et al., <i>Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings</i>, <i>Advanced Drug Delivery Reviews</i>, Vol. 23: 3-25, 1997</p>								
<p>Lombardo, F., et al., <i>ElogP_{oct}: A tool for lipophilicity determination in drug discovery</i>, <i>J. Med. Chem.</i>, Vol. 43(15): 2922-2928, 2000</p>								
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<p>EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.</p>								

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Lombardo, F., et al., <i>ElogD_{oct}: A tool for lipophilicity determination in drug discovery. 2. Basic and neutral compounds</i> , <u>J. Med. Chem.</u> , Vol. 44(15): 2490-2497, 2001										
Lüllmann, H., et al., <i>The binding of drugs to different polar lipids in vitro</i> , <u>Biochem. Pharmacol.</u> , Vol. 28: 3409-3415, 1979										
Maillard, C., et al., <i>Design, synthesis, and pharmacological evaluation of conformationally constrained analogues of N,N-diaryl- and N-Aryl-N-alkylguanidines as potent inhibitors of neuronal Na⁺ channels</i> , <u>J. Med. Chem.</u> , Vol. 41, 3048-3061, 1998										
Manners, C., et al., <i>Lipophilicity of zwitterionic sulphate conjugates of tiaramide, propranolol and 4'-hydroxypropranolol</i> , <u>Xenobiotica</u> , Vol. 19(12): 1387-1397, 1989										
Melander, W., et al., <i>Stationary phase effects in reversed-phase chromatography I. Comparison of energetics of retention on alkyl-silica bonded phases</i> , <u>J. Chromatogr.</u> , Vol. 199: 35-56, 1980										
Meulermans, W., <i>Plasma protein binding and distribution of fentanyl, sufentanil, alfentanil and lofentanil in blood</i> , <u>Arch. Int. Pharmacodyn.</u> , Vol. 257: 4-19, 1982										
Minick, D., et al., <i>Modeling octanol-water partition coefficients by reversed-phase liquid chromatography</i> , <u>J. Chromatogr.</u> , Vol. 461: 177-191, 1989										
Minick, D., et al., <i>A comprehensive method for determining hydrophobicity constants by reversed-phase high-performance liquid chromatography</i> , <u>J. Med. Chem.</u> , Vol. 31: 1923-1933, 1988										
Mohler, V., et al., <i>On Chemistry and synthesis of 3,7-dimethyl-1-(5-oxo-hexyl)-xanthine</i> , <u>Arzneim.-Forsch.</u> , Vol. 21: 1159-1160, 1971										
Morelock, M., et al., <i>Estimation and correlation of drug water solubility with pharmacological parameters required for biological activity</i> , <u>J. of Pharm. Sci.</u> , Vol. 83(7): 948-952, 1994										
Müller, W., et al., <i>Interactions of benzodiazepines with human serum albumin, Circular Dichroism Study</i> , <u>Arch. Pharmacol.</u> , Vol. 278: 301-312, 1973										
O'Connor, D., et al., <i>Influence of physicochemistry on the brain penetration of the triptans in rat</i> , <u>Poster presented at the XIV Course in Drug Research</u> , Helsinki, Finland, June 5-6, 1997										
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OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)												
		Okada, J., et al., ¹³ C nuclear magnetic resonance spectra of antipyrine derivatives and their application to hansch analysis, <u>Chem. Pharm. Bull.</u> , Vol. 24(1): 61-71, 1976										
		Pagliara, A., et al., Structural properties governing retention mechanisms on RP-HPLC stationary phases used for lipophilicity measurements, <u>Journal of Liquid Chromatography</u> , Vol. 18(9): 1721-1745, 1995										
		Pauletti, G., et al., Can counterions affect the transport of a lipophilic diarylguanidine (CNS 1237) across caco-2 cell monolayers in vitro?, <u>Pharm. Res.</u> , Vol. 14: S-24, 1997										
		Perlman, M., et al., Use of pH dependence of log D for PKA determination and formulation of diarylguanidines, <u>Pharm. Res.</u> , Vol. 13: S-339, 1996										
		Priewer, H., et al., Solubility and distribution coefficient of potassium and magnesium retaining triamterene derivatives, <u>Pharmazie</u> , Vol. 51: 279-282, 1996										
		Sangster, J., <u>Octanol-water partition coefficients: Fundamentals and Physical Chemistry</u> , Wiley, New York, 79-112, 1997										
		Scherrer, R., et al., Use of distribution coefficients in quantitative structure-activity relationships, <u>J. Med. Chem.</u> , Vol. 20(1): 53-58, 1977										
		Schutz, V., et al., Screening, detection and biotransformation of Lormetazepam, a new hypnotic agent from the 1,4-benzodiazepine series, <u>Arzneim.-Forsch.</u> , Vol. 32: 177-183, 1977										
		Seiler, P., et al., 5-Phenyl-1,3-dihydro-1,4-benzodiazepin-2-ones, Experimental verification of substituent constants, <u>Arzneim.-Forsch./Drug Res.</u> , Vol. 33: 1519-1522, 1983										
		Sirius Technical Application Notes, Sirius Analytical Instruments, Ltd., Forest Row, East Sussex RH18 5DW, Vol. 1: pages 2, 3, 8, 84, 85, 86, 99b, 99c, 122 & 123, 1994										
		Sirius Technical Application Notes, Sirius Analytical Instruments, Ltd., Forest Row, East Sussex RH18 5DW, Vol. 2: pages 36, 37, 81, 82, 83, 84, 114, 115, 167 & 168, 1995										
		Slater, B., et al., pH-metric log P. 4. Comparison of partition coefficients determined by HPLC and potentiometric methods to literature values, <u>J. Pharm. Sci.</u> , Vol. 83(9): 1280-1283, 1994										
		Smith, D., et al., Physicochemical properties in drug metabolism and pharmacokinetics, <u>Computer-Assisted Lead Finding and Optimization</u> , Ch. 17: 265-276, 1997										
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		Smith, D., et al., <i>Design of drugs involving the concepts and theories of drug metabolism and pharmacokinetics</i> , <u>Medicinal Research Reviews</u> , Vol. 16(3): 243-266, 1996								
		Stopher, D., et al., <i>An improved method for the determination of distribution coefficients</i> , <u>J. Pharm. Pharmacol.</u> , Vol. 42: 144, 1989								
		Taylor, P., <i>Hydrophobic properties of drugs</i> , In <u>Comprehensive Medicinal Chemistry</u> , Vol. 5: 241-294, 1990								
		ter Laak, A., et al., <i>Lipophilicity and hydrogen-bonding capacity of H₁-antihistaminic agents in relation to their central sedative side-effects</i> , <u>Eur. J. Pharm. Sci.</u> , Vol. 2: 373-384, 1994								
		Timmermans, P., et al., <i>Lipophilicity and brain disposition of clonidine and structurally related imidazolines</i> , <u>Naunyn-Schmiedeberg's Arch. Pharmacol.</u> , Vol. 300: 217-226, 1977								
		Tomida, H., et al., <i>Solubilization of steroid hormones by polyxyethylene lauryl ether</i> , <u>Chem. Pharm. Bull.</u> , Vol. 26(9): 2832-2837, 1978								
		Tsai, R., et al., <i>Influences of stereochemical factors on the partition coefficient of diastereomers in a biphasic octan-1-ol/water system</i> , <u>J. Chem. Res. (M)</u> : 1901-1920, 1993								
		Ungell, A., et al., <i>Membrane transport of drugs in different regions of the intestinal tract of the rat</i> , <u>J. Pharm. Sci.</u> , Vol. 87(3): 360-366, 1998								
		Unger, S., et al., <i>Octanol-physiological buffer distribution coefficients of lipophilic amines by reversed-phase high-performance liquid chromatography and their correlation with biological activity</i> , <u>J. Med. Chem.</u> , Vol. 24: 262-270, 1981								
		Valko, K., et al., <i>Chromatographic hydrophobicity index by fast-gradient RP-HPLC: A high-throughput alternative to log P/log D</i> , <u>Analytical Chemistry</u> , Vol. 69(11): 2022-2029, 1997								
		Van de Waterbeemd, H. et al., <i>Lipophilicity measurements by reversed-phase high performance liquid chromatography (RP-HPLC)</i> , <u>Lipophilicity in Drug Action and Toxicology</u> , Ch. 5: 73-87, 1996								
		Winiwarter, S., et al., <i>Correlation of human jejunal permeability (in vivo) of drugs with experimentally and theoretically derived parameters. A multivariate data analysis approach</i> , <u>J. Med. Chem.</u> , Vol. 41: 4939-4949, 1998								
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